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STUDIES IN HYPERTENSION

# Patterns of Left Ventricular Hypertrophy and Geometric Remodeling In Essential Hypertension

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**The spectrum of left ventricular geometric adaptation to hypertension was investigated in 165 patients with untreated essential hypertension and 125 age- and gender-matched normal adults studied by two-dimensional and M-mode echocardiography. Among hypertensive patients, left ventricular mass index and relative wall thickness were normal in 52%, whereas 13% had increased relative wall thickness with normal ventricular mass ("concentric remodeling"), 27% had increased mass with normal relative wall thickness (eccentric hypertrophy) and only 8% had "typical" hypertensive concentric hypertrophy (increase in both variables).**

**Systemic hemodynamics paralleled ventricular geometry, with the highest peripheral resistance in the groups with concentric remodeling and hypertrophy, whereas cardiac index was supernormal in those with eccentric hypertrophy and low normal in patients with concentric remodeling. The left ventricular short-axis/long-axis ratio was positively related to stroke volume ($r = 0.45$, $p < 0.001$), with cavity shape most elliptic in patients with concentric remodeling and most spheric in those with eccentric hypertrophy. Normality of left ventricular mass in concentric remodeling appeared to reflect offsetting by volume "underload" of the effects of pressure overload, whereas eccentric hypertrophy was associated with concomitant pressure and volume overload.**

**Thus, arterial hypertension is associated with a spectrum of cardiac geometric adaptation matched to systemic hemodynamics and ventricular load. Concentric left ventricular remodeling and eccentric hypertrophy are more common than the typical pattern of concentric hypertrophy in untreated hypertensive patients.**

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The left ventricle is generally thought to adapt to sustained arterial hypertension by developing concentric hypertrophy (1,2). According to the paradigm of compensatory ventricular response to a chronic pressure overload, ventricular wall thickness should increase proportionally to blood pressure level to maintain normal wall stress (1); left ventricular dilation is considered to represent a late transition toward myocardial failure (2).

However, left ventricular adaptation to human hypertension has been shown to be more complex than expected. In fact, many patients with mild to moderate hypertension exhibit normal left ventricular mass and wall thickness (3–6); other hypertensive patients have eccentric ventricular hypertrophy that is not related to systolic dysfunction, but rather to increased cardiac output and preload (5,7). Conversely, we have observed increases in absolute and relative wall thickness with normal ventricular mass in some hypertensive patients, a pattern we term "concentric remodeling." Although there is some evidence that the spectrum of cardiac adaptation to hypertension may be related to differences in hemodynamic load (5,7,8) or in myocardial contractile state (5,6,8–10), no study has extensively investigated the spectrum of changes in left ventricular structure and their possible pathophysiologic mechanisms in human hypertension.

In the present study, we used echocardiographically derived left ventricular mass and relative wall thickness to assess the patterns of ventricular geometric adaptation to systemic hypertension and their relations to systemic hemodynamics, left ventricular load and contractile performance.

## Methods

**Study subjects.** Data were obtained from 165 patients with borderline to severe essential hypertension and 125

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normal subjects. Part of the study group (101 normal and 71 hypertensive subjects) was studied at the New York Hospital-Cornell Medical Center and the remainder (24 normal and 94 hypertensive subjects) at the Clinical Medicine Institute of the University of Sassari (Sassari, Italy) under protocols approved by the respective Human Research Committees at regular intervals since 1979. Data from 50 normotensive and 50 hypertensive subjects studied at Cornell have been previously reported in part (8). Hypertensive patients had clinic blood pressure measurements by mercury manometer >140/90 mm Hg on three measurements taken at 1-week intervals in the absence of any previous antihypertensive treatment to exclude pharmacologic effects on hemodynamics or ventricular hypertrophy and function. Patients who had evidence of secondary hypertension, valvular, coronary or primary myocardial disease, serum creatinine >2 mg/dl or age >74 years were excluded. Normal subjects had multiple blood pressure measurements <140/90 mm Hg and were in the same age range as the hypertensive patients. Gender and race were similar in normotensive and hypertensive groups. Body mass index (weight in kg/[height in m]$^2$) was calculated as an index of obesity.

*Blood pressure measurements* used in the study were taken with a mercury sphygmomanometer at the time of echocardiography with the patient supine. Systolic and diastolic pressures were taken as the first and fifth phases of the Korotkoff sounds. Ambulatory 24-h blood pressure recordings were performed on a working day in 26 normal and 42 hypertensive subjects within 2 weeks of the echocardiographic examination by a fully automatic recorder (IRC 5200, Spacelabs). Daytime and nighttime blood pressures were determined as median measurements of at least three technically satisfactory readings in each setting.

**Echocardiography.** Two-dimensionally guided M-mode echocardiograms were performed on each subject by expert sonographers using commercially available echocardiographs with 2.25- to 3-MHz transducers. Tracings were recorded on stripchart paper at 50 mm/s. They were analyzed without knowledge of other data by two readers. Measurements were taken at or just below the tip of the mitral valve by using a graph pen interfaced to a computer. Left ventricular internal dimension and septal and posterior wall thicknesses were measured at end-diastole and end-systole, according to the American Society of Echocardiography guidelines (11), and used for all purposes except determination of ventricular mass. Left ventricular mass was calculated at end-diastole by using the Penn convention (12,13). Relative wall thickness was measured at end-diastole as the ratio of 2 × (posterior wall thickness/internal dimensions). Fractional shortening was assessed as a measure of ejection phase performance. Left ventricular volumes were estimated from end-diastolic and end-systolic dimensions by using the Teichholz formula (14); left ventricular volumes, stroke volume and cardiac output determined by this method have been shown to be accurate in patients with symmetrically contracting ventricles (15–17), as was verified by two-dimensional echocardiography in all of our patients.

Total peripheral resistance was assessed as ([mean arterial blood pressure × 80]/cardiac output); mean blood pressure was estimated as 1/3 pulse pressure + diastolic pressure. End-systolic meridional wall stress was calculated from end-systolic echocardiographic ventricular dimensions and thicknesses and from simultaneously measured systolic blood pressure by a catheterization-validated formula (18). Fractional shortening as a percent of that predicted for end-systolic stress in normal subjects (9) was calculated as an index of left ventricular contractile performance; according to the regression equation between end-systolic stress and fractional shortening obtained in 125 normal subjects, predicted fractional shortening = 98.3 − (14.8 natural log[end-systolic stress]).

**Echocardiographic measurements of left ventricular geometry.** Two-dimensional echocardiograms were quantitated in 50 normal subjects and 50 hypertensive patients who had high quality two-dimensional images to obtain more complete characterization of left ventricular geometry. Wide angle two-dimensional views from these subjects were recorded on 0.5-in. (1.27-cm) videotapes and analyzed with a computerized system. Two-dimensional short-axis images were obtained at the papillary muscle level; long-axis images were recorded in apical two- and four-chamber views. A single reader performed two-dimensional measurements without knowledge of blood pressure level and M-mode findings. Videotapes were reviewed in real time, slow motion and frame by frame until the best definition of endocardial and epicardial contours was reached. At least four stop frame images were used to obtain average measurements of total, cavity and myocardial cross-sectional areas, as well as left ventricular long-axis dimensions at end-diastole (Q wave on the electrocardiogram) and end-systole (the smallest cavity area). Left ventricular endocardial contours were assessed from parasternal short-axis views at the papillary muscle level. Contours were traced on the monitor by using a graphic tablet. Endocardial echoes were excluded from the left ventricular cavity area (Ac), according to the black-white method of interface identification. The left ventricular long axis (L) was measured from the apical endocardium to the midpoint of the mitral valve plane in the apical four-chamber view. From these direct measurements, we derived the major (a) and the minor (b) hemiaxes, where $a = L/2$; $b = \sqrt{Ac/3.14}$. Left ventricular chamber shape was quantitatively described by the ratio of minor to major hemiaxis (b/a ratio) (19,20), which reflects the degree of sphericity (or ellipticness) of the cavity. Left ventricular volumes were obtained at end-diastole and end-systole with the biplane ellipsoid method (21), where Ventricular volume = $\pi/6 \times L \times D1 \times D2$, where L is the long axis and D1 and D2 are the right-left and the anteroposterior minor axis, respectively. Two-dimensional echocardiographic stroke volume was calculated as the difference between end-diastolic and end-

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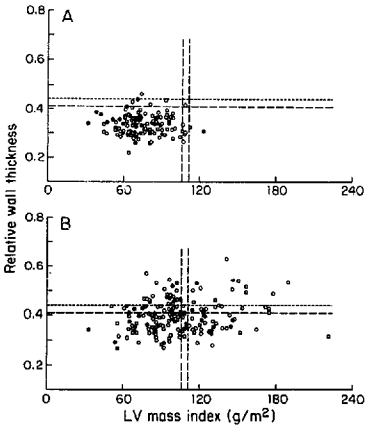


**Figure 1.** Diagrams divided into four fields by the upper 95% confidence limits of left ventricular (LV) mass index in 225 normal adults (111 g/m² in men and 106 g/m² in women, **right and left dashed vertical lines**, respectively) and of relative wall thickness (0.41 for both men and women, **dashed horizontal line**); we used a second, more restrictive cutpoint of relative wall thickness, which approximates the upper 99% confidence limit (0.44, **dotted horizontal line**). The four fields correspond to different patterns of left ventricular geometry; normal left ventricle (**bottom left**), concentric remodeling (**top left**), concentric hypertrophy (**top right**) and eccentric hypertrophy (**bottom right**). **A,** Data from 125 normal subjects (89 men [**open circles**] and 36 women [**closed circles**]); 98% of them exhibit normal ventricular geometry when a relative wall thickness cutpoint of 0.44 is used. **B,** Data points for 165 hypertensive subjects (125 men [**open circles**] and 40 women [**closed circles**]).

systolic volumes, and multiplied by heart rate to derive cardiac output.

**Patterns of left ventricular geometry.** Four different patterns of left ventricular anatomic adaptation to hypertension were identified by categorizing patients according to values of end-diastolic relative wall thickness and left ventricular mass index (5,22) (Fig. 1). Upper normal limits for left ventricular mass index (estimated as 2 SD above the mean values in 225 normal subjects concurrently studied with the same M-mode and two-dimensional echocardiographic methods and identical reading criteria) were 111 g/m² in men and 106 g/m² in women. Elevated relative wall thickness with increased mass index identified the presence of concentric as opposed to eccentric hypertrophy (1,22–25) and in the presence of normal left ventricular mass identified concentric left ventricular remodeling. A partition value of 0.44 for relative wall thickness was used for both men and women chosen to represent approximately the 99th percentile value in these normal subjects to maintain acceptably high specificity for detection of abnormal ventricular geometry by either or both of the two measures of ventricular anatomy. This partition value is close to previously reported upper normal limits of relative wall thickness measured by independent M-mode echocardiography (22,26). A second lower relative wall thickness cutpoint of 0.41 was also utilized, representing the 95th percentile of the normal values as a less restrictive criterion for inclusion of cases in concentric remodeling and hypertrophy subgroups.

**Statistical methods.** Data were stored and analyzed by the CLINFO statistical system (27) of the Cornell Medical College Clinical Research Center. Relations between variables were assessed using linear regression analysis and Pearson's correlation coefficient. Comparisons between two groups were performed by unpaired *t* test, and differences among more than two groups were tested by one-way analysis of variance, followed by the Newman-Keuls posthoc test (28). Data are expressed as mean value ± 1 SD.

## Results

**Clinical and echocardiographic characteristics of normal and hypertensive subjects (Table 1 and 2).** There were no statistical differences in age, gender, race or body surface area between normal and hypertensive subjects either in the entire study group (Table 1) or in the subset studied in detail by two-dimensional echocardiography. Compared with the normal subjects, hypertensive patients had significantly higher ($p < 0.01$) systolic and diastolic blood pressure, body mass index, cardiac index, total peripheral resistance, posterior wall thickness, relative wall thickness and left ventricular mass index (Table 2). Left ventricular diastolic dimension, peak and end-systolic meridional wall stress, fractional

**Table 1.** Characteristics of 125 Normal and 165 Hypertensive Subjects

| | Age (yr) | Gender (male/female) | Race (white/black) | BSA (m²) | BMI (kg/m²) | Blood Pressure at the Time of Echocardiography (mm Hg) | |
|---|---|---|---|---|---|---|---|
| | | | | | | Systolic | Diastolic |
| Normal subjects | 44 ± 13 | 89/36 | 120/5 | 1.9 ± 0.2 | 24.9 ± 4 | 124 ± 10 | 77 ± 7 |
| Hypertensive patients | 45 ± 12 | 125/40 | 156/9 | 1.8 ± 0.2 | 26.4 ± 3* | 152 ± 21* | 100 ± 13* |

*$p < 0.01$. BMI = body mass index; BSA = body surface area.

**Table 2.** Echocardiographic Data in 125 Normal and 165 Hypertensive Subjects

| | Normal Subjects | Hypertensive Patients |
|---|---|---|
| Posterior wall thickness (cm) | 0.84 ± 0.1 | 1.1 ± 0.1† |
| Left ventricular diastolic internal diameter (cm) | 5 ± 0.5 | 5.1 ± 0.5 |
| Relative wall thickness | 0.33 ± 0.04 | 0.4 ± 0.07† |
| Left ventricular mass index (Penn) (g/m$^2$) | 75 ± 17 | 104 ± 31† |
| Stroke index (ml/min per m$^2$) | 43 ± 9 | 45 ± 11 |
| Cardiac index (liters/min per m$^2$) | 2.9 ± 0.8 | 3.1 ± 0.8† |
| Total peripheral resistance (dynes·s·cm$^{-5}$) | 1,486 ± 386 | 1,735 ± 490† |
| End-systolic meridional wall stress (10$^3$ dynes/cm$^2$) | 67 ± 17 | 68 ± 21 |
| Fractional shortening (%) | 37 ± 5 | 37 ± 7 |
| Afterload-corrected fractional shortening (% of predicted) | 100 ± 9 | 101 ± 12 |
| Left ventricular diastolic minor/major hemiaxis ratio (n = 50) | 0.59 ± 0.06 | 0.57 ± 0.05 |
| Left ventricular systolic minor/major-hemiaxis ratio (n = 50) | 0.53 ± 0.07 | 0.49 ± 0.06* |

*p < 0.05; †p < 0.01.

shortening and afterload-corrected fractional shortening were not statistically different in the two groups. In the subgroups of 50 normal and 50 hypertensive subjects who were studied in detail by two-dimensional echocardiography, diastolic cavity shape (minor/major hemiaxis ratio) was similar; hypertensive subjects had more elliptic left ventricular systolic shape (p < 0.05) (Table 2).

**Patterns of left ventricular geometry.** Of the 125 normal subjects, 122 (98%) had both normal left ventricular mass by gender-specific criteria and normal relative wall thickness when 0.44 was used as a partition value. When the relative wall thickness partition value was lowered to 0.41, 117 (94%) of normal adults were classified as normal by both indexes of ventricular geometry (Fig. 1). Four different groups were identified when the 165 hypertensive patients were categorized according to a relative wall thickness value of 0.44 and gender-specific ventricular mass index partitions (Fig. 1). Of the 165 hypertensive patients, 87 (52%) had both ventricular mass and relative wall thickness within normal limits. In 21 patients (13%), left ventricular mass was normal but relative wall thickness was increased; thus 20% of the hypertensive patients with normal left ventricular mass exhibited concentric remodeling of the left ventricle. Among those with increased left ventricular mass index, relative wall thickness was high in 13 patients or 8% of the total study group (concentric hypertrophy) and normal in 44 or 27% of the total group who exhibited eccentric hypertrophy. Use of the lower relative wall thickness partition value of 0.41 decreased the proportions of patients with normal left ventricular geometry (n = 72 or 44%) or eccentric hypertrophy (n = 32 or 19%) and increased the number with concentric remodeling (n = 36 or 22%) or hypertrophy (n = 25 or 15%).

**Table 3.** Hemodynamics, Left Ventricular Load and Systolic Performance Associated With Different Left Ventricular Geometric Patterns in 165 Hypertensive Patients

| | Hypertensive Patients | | | |
|---|---|---|---|---|
| | Normal Left Ventricle (n = 87) | Concentric Remodeling (n = 21) | Concentric Hypertrophy (n = 13) | Eccentric Hypertrophy (n = 44) |
| Age (yr) | 43 ± 11 | 50 ± 10 | 50 ± 15 | 45 ± 11 |
| Body surface area (m$^2$) | 1.9 ± 0.3 | 1.9 ± 0.2 | 1.8 ± 0.6 | 1.8 ± 0.4 |
| Body mass index (kg/m$^2$) | 26.5 ± 4.1 | 26.3 ± 3.4 | 26 ± 3.2 | 26.2 ± 2.9 |
| Gender (male/female) | 68/19 | 15/6 | 11/2 | 31/13 |
| Duration (mo) | 24 ± 32 | 8 ± 9 | 31 ± 29 | 28 ± 57 |
| Heart rate (beats/min) | 70 ± 13 | 70 ± 10 | 71 ± 10 | 71 ± 10 |
| Systolic pressure (mm Hg) | 145 ± 16* | 153 ± 21* | 170 ± 34*†‡ | 157 ± 22*†§ |
| Diastolic pressure (mm Hg) | 97 ± 12* | 100 ± 13* | 110 ± 20*†‡ | 102 ± 12*†§ |
| Posterior wall thickness (cm) | 0.9 ± 0.09* | 1.1 ± 0.07*† | 1.3 ± 0.09*†‡ | 1 ± 0.69*†§ |
| Diastolic dimension (cm) | 5 ± 0.4 | 4.5 ± 0.3*† | 4.9 ± 0.3‡ | 5.6 ± 0.5*†‡§ |
| Relative wall thickness (cm) | 0.36 ± 0.04* | 0.49 ± 0.03*† | 0.52 ± 0.04*† | 0.38 ± 0.04*‡§ |
| Left ventricular mass index (g/m$^2$) | 85 ± 17 | 93 ± 9* | 144 ± 23*†‡ | 136 ± 27*†‡ |
| Stroke index (ml/m$^2$) | 42 ± 9 | 35 ± 8*† | 44 ± 9‡ | 54 ± 9*†‡§ |
| Cardiac index (liters/min per m$^2$) | 2.9 ± 0.7 | 2.4 ± 0.5*† | 3.1 ± 0.8‡ | 3.8 ± 0.7*†‡§ |
| Total peripheral resistance (dynes·s·cm$^{-5}$) | 1,741 ± 407* | 2,217 ± 637*† | 1,992 ± 513*†‡ | 1,417 ± 289*‡§ |
| End-systolic wall stress (10$^3$ dynes/cm$^2$) | 71 ± 16 | 52 ± 18*† | 53 ± 12*† | 74 ± 27‡§ |
| Fractional shortening (%) | 36 ± 6 | 39 ± 8 | 39 ± 7 | 37 ± 7 |
| Afterload-corrected fractional shortening (%) | 101 ± 11 | 95 ± 14 | 96 ± 12 | 104 ± 13‡§ |

*p < 0.05 versus normal subjects; †p < 0.05 versus hypertensive patients with a normal left ventricle; ‡p < 0.05 versus concentric remodeling; §p < 0.05 versus concentric hypertrophy.

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**Table 4.** Two-Dimensional Echocardiographic Indexes of Left Ventricular Geometry and Load Associated With Different Left Ventricular Patterns in 50 Hypertensive Patients

| | | Hypertensive Patients | | |
|---|---|---|---|---|
| | Normal Left Ventricle | Concentric Remodeling | Concentric Hypertrophy | Eccentric Hypertrophy |
| No. of patients | 27 | 11 | 6 | 6 |
| Diastolic minor/major hemiaxis ratio | 0.57 ± 0.04 | 0.52 ± 0.04* | 0.6 ± 0.04‡ | 0.63 ± 0.03†‡ |
| Systolic minor/major hemiaxis ratio | 0.5 ± 0.05 | 0.46 ± 0.06 | 0.53 ± 0.06 | 0.51 ± 0.07 |
| Stroke index (ml/m$^2$) | 38 ± 8 | 32 ± 3 | 45 ± 10*†‡ | 53 ± 9*†‡§ |
| Cardiac index (liters/min per m$^2$) | 2.5 ± 0.6 | 2.3 ± 0.4 | 3 ± 0.9* | 3.8 ± 0.8*†‡§ |
| Total peripheral resistance (dyne·s·cm$^{-5}$) | 1,760 ± 482* | 1,896 ± 339* | 1,673 ± 490* | 1,213 ± 164†‡§ |

*p < 0.05 vs. normal subjects; †p < 0.05 vs. hypertensive patients with a normal left ventricle; ‡p < 0.05 vs. concentric remodeling; §p < 0.05 vs. concentric hypertrophy.

**Relation of ventricular geometric pattern to hemodynamics, load and systolic performance (Tables 3 to 5).** There were no significant differences among the four groups in age, gender, body surface area, body mass index, heart rate or duration of hypertension. The group with normal ventricular structure was characterized by mildly increased systolic and diastolic blood pressure and total peripheral resistance. Left ventricular diastolic diameter, relative wall thickness, mass index, cavity shape, fractional shortening, afterload-corrected fractional shortening, end-systolic wall stress and cardiac index were all normal.

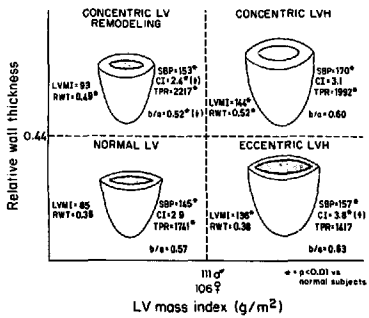
*The group with concentric left ventricular remodeling* had moderately increased systolic and diastolic blood pressure and the highest total peripheral resistance of any group in this study (Table 3). Left ventricular wall thickness was mildly increased compared to that in both normotensive subjects and hypertensive patients with normal ventricular geometry. Despite the increased pressure load and lack of increased myocardial mass, end-systolic meridional wall stress was subnormal, showing that optimal or even over-compensatory left ventricular mechanical adaptation had been achieved. Left ventricular end-diastolic dimension was reduced in this group, suggesting that pressure overload was also balanced by diminished volume load; consistent with this interpretation, stroke index and cardiac index were lower than in normal subjects. In this group, the diastolic minor/major-hemiaxis ratio was significantly reduced, indicating that the left ventricular cavity shape was more elliptic (Fig. 2); fractional shortening and afterload-corrected fractional shortening were normal. Ambulatory 24-h blood pressure recordings were available in 24 patients with normal ventricular geometry and in 13 with concentric remodeling. Although both groups had a higher average daytime blood pressure than that observed in 26 normotensive subjects, only patients with concentric ventricular remodeling had elevated nighttime blood pressure (Table 5).

**Table 5.** Casual and 24-h Ambulatory Blood Pressure in 26 Normotensive Subjects and 37 Hypertensive Patients With Normal Left Ventricular Geometry or Concentric Remodeling

| | | Hypertensive Patients | |
|---|---|---|---|
| | Normotensive Subjects (n = 26) | Normal Geometry (n = 24) | Concentric Remodeling (n = 13) |
| Casual blood pressure (mm Hg) | | | |
| Systolic | 130 ± 9 | 146 ± 8* | 150 ± 10* |
| Diastolic | 84 ± 7 | 94 ± 6* | 96 ± 7* |
| Daytime blood pressure (mm Hg) | | | |
| Systolic | 127 ± 9 | 141 ± 11* | 147 ± 10* |
| Diastolic | 78 ± 7 | 92 ± 8* | 95 ± 7* |
| Sleep blood pressure (mm Hg) | | | |
| Systolic | 109 ± 11 | 113 ± 15 | 122 ± 11* |
| Diastolic | 67 ± 6 | 69 ± 7 | 75 ± 8*† |

*p < 0.01 vs. normotensive subjects; †p < 0.05 vs. patients with normal left ventricular geometry.

**Figure 2.** Hemodynamic and geometric profiles in hypertensive patients with the four patterns of left ventricular (LV) geometry. The short-axis/long-axis ratio (b/a) was derived by two-dimensional echocardiography. CI = cardiac index (liters/min per m$^2$); LVH = left ventricular hypertrophy; LVMI = left ventricular mass index (g/m$^2$); RWT = relative wall thickness; SBP = systolic blood pressure; TPR = total peripheral resistance (dynes·s·cm$^{-5}$).



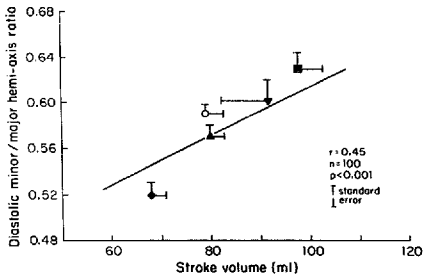



**Figure 3.** Stroke volume and left ventricular cavity shape (minor/major hemiaxis ratio at end-diastole) measured by two-dimensional echocardiography are positively related in 50 normal subjects (**open circle**) and 50 hypertensive subjects. Hypertensive patients are categorized into groups with normal geometry (**solid upright triangle**), concentric remodeling (**solid diamond**), concentric hypertrophy (**solid inverted triangle**) or eccentric hypertrophy (**solid square**).

The group of patients with concentric hypertrophy had elevated blood pressure and total peripheral resistance, as well as a slight increase in cardiac index (Table 3). End-systolic meridional wall stress was subnormal (Table 3), suggesting that hypertrophy was appropriate or even supercompensatory in relation to rest blood pressure; left ventricular diastolic dimension, cavity shape, fractional shortening and stress-adjusted fractional shortening were normal. Patients with eccentric hypertrophy had increased systolic and diastolic blood pressure, high cardiac index and normal total peripheral resistance. The left ventricular chamber was mildly dilated and more spheric and end-systolic meridional wall stress was increased, suggesting inadequate hypertrophy; despite a high level of afterload, fractional shortening and stress-adjusted fractional shortening were normal. Only two patients with concentric and three with eccentric hypertrophy had ambulatory 24-h blood pressure recordings, too few to allow analysis of daytime or nighttime blood pressure profiles. In the four groups of hypertensive patients, left ventricular fractional shortening as a percent of the predicted value paralleled end-diastolic chamber diameter, with highest values for both variables in patients with eccentric hypertrophy and lowest in those with concentric remodeling, suggesting an influence of preload on this index of ventricular contractile performance.

Hemodynamics, left ventricular geometry, volume load and systolic performance were also examined in groups obtained using the second, lower cutpoint of relative wall thickness (0.41 vs. 0.44) to identify concentric left ventricular remodeling or concentric hypertrophy. The main features associated with the four patterns were substantially the same using this less restrictive criterion, except for the higher proportion of patients assigned to the concentric remodeling or hypertrophy groups (22% and 15%, respectively) and the smaller proportion who exhibited normal ventricular geometry (44%) or eccentric hypertrophy (19%).

**Left ventricular shape in patients with different geometric patterns.** Among the 100 subjects studied in detail by two-dimensional echocardiography, the sphericity index was directly related to stroke volume measured by two-dimensional echocardiography ($r = 0.45$; $p < 0.001$) (Fig. 3), suggesting an interplay between ventricular shape and filling or contraction. Patients with eccentric hypertrophy showed the highest stroke volume and most spheric left ventricular cavity; patients with concentric remodeling exhibited the lowest stroke volumes and most elliptic left ventricular shape.

**Potential limitations.** A potential methodologic limitation should be taken into account because underestimation of left ventricular volume might occur using the Teichholz formula in patients with an extremely elliptic ventricular shape (long axis/minor axis ratio > 3 or b/a ratio < 0.33) (15). However, this is not likely to be the case in our patients with concentric ventricular remodeling, who had b/a ratios at end-diastole (0.47 to 0.56) and end-systole (0.39 to 0.52) within the 95% confidence limits for the normal subjects (0.45 to 0.71 in diastole and 0.39 to 0.66 in systole) (Tables 2 and 4). Moreover, stroke volume as obtained by two-dimensional echocardiography, which incorporates both the long and the minor axis in the formula, was closely related to that obtained from M-mode left ventricular minor-axis dimensions in the Teichholz regression equation ($r = 0.72$, SEE = 12 ml, $p < 0.001$). These observations suggest that measurements of stroke volume by M-mode echocardiography and the Teichholz formula, as well as derived measures of systemic hemodynamics were not likely to be unreliable because of geometric abnormalities in our series.

Another methodologic limitation is that Doppler echocardiography was not used to eliminate the possibility of regurgitant lesions, which might contribute to the eccentric hypertrophy in some patients. However, our experience in patients recently studied by Doppler methods is that aortic regurgitation or more than trivial mitral regurgitation is rare in hypertensive patients <60 years of age. The young age of our subjects (mean 45 years) and exclusion of any subject with a murmur suggesting valvular regurgitation make it unlikely this possibility had an important influence on our findings.

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## Discussion

**Patterns of left ventricular geometry.** Although one might expect that patients with high blood pressure would uniformly develop concentric left ventricular hypertrophy proportional to the level of blood pressure (1,2), numerous studies (3–5,7–9,29–31) indicate this is often not the case. We recently reported (8) that left ventricular mass is more closely related to ventricular cavity size than to systolic blood pressure (8) and that both volume load and myocardial contractile state may play an important role in determining the left ventricular adaptation to hypertension.

Data in the present study of 125 normotensive and 165 hypertensive adults show that left ventricular adaptation to hypertensive pressure overload is quite complex, concentric hypertrophy representing only one and not the most frequent of the observed patterns. We assessed left ventricular anatomy not only as ventricular weight (mass), but also by using the relation of muscle thickness to cavity size (relative wall thickness) as a sensitive indicator of the geometric pattern of hypertrophy (1,22–25). Using this approach and criteria with high specificity (122 of 125 [97.5%]) in normal subjects, we were able to identify four different left ventricular anatomic patterns in patients with high blood pressure (Fig. 1). Eighty-seven hypertensive patients (52%) had completely normal ventricular mass and relative wall thickness; 21 (13%) had increased relative wall thickness with normal ventricular mass—a pattern we term concentric remodeling—whereas 13 (8%) had concentric and 44 (27%) had eccentric left ventricular hypertrophy.

### *Ventricular Geometry, Hemodynamics, Load and Systolic Performance*

Left ventricular geometry, hemodynamics, load and contractile performance were notably different among the four groups.

**Normal left ventricular geometry group.** Total peripheral resistance and systolic and diastolic blood pressure were only slightly increased in the first group, whereas left ventricular geometry, load and systolic function were virtually normal. In the 24 patients in this group who had ambulatory 24-h blood pressure recordings, average daytime blood pressure was slightly elevated and nighttime blood pressure was normal (Table 5), suggesting that normality of cardiac structure and function is compatible with mild and intermittent pressure overload.

**Concentric remodeling group.** Despite similarly normal left ventricular mass, the second group had distinctive geometric and hemodynamic characteristics that have not been previously described. Increased relative wall thickness, accompanied by more elliptic ventricular chamber shape but normal left ventricular mass was observed in 21 (13%) of the 165 hypertensive patients (Fig. 2), suggesting that concentric remodeling of the left ventricle without appreciable hypertrophy occurs in a subset of hypertensive patients. Rest blood pressure was high, cardiac index was reduced and peripheral resistance attained the highest values observed among the hypertensive groups; both average daytime and nighttime pressures were elevated in the 13 patients with ambulatory 24-h blood pressure recordings (Table 5). In this group, average left ventricular posterior wall thickness was slightly but significantly increased compared with that in both normotensive and hypertensive subjects with normal ventricular geometry (Table 3). Diminished left ventricular cavity size, which paralleled decreased stroke volume, also contributed to elevated relative wall thickness and reduced wall tension. Because end-systolic meridional wall stress was low in this group, concentric remodeling seems to blunt the stimulus to increase left ventricular mass due to hypertensive overload.

The stimulus to increased relative wall thickness in the concentric remodeling group is unknown, although reduced arterial compliance—suggested by the subnormal stroke volume and slightly high pulse pressure in these patients (32)—or elevated diastolic blood pressure at night or during everyday activities, which we have shown to be closely related to relative wall thickness (29), are attractive possibilities. Alternatively, in a separate series of 68 untreated patients with essential hypertension, the positive relations we recently observed (33) between plasma volume determined by $^{125}$I serum albumin and echocardiographic measurements of left ventricular stroke volume, diastolic dimension and mass ($r = 0.43$ to $0.53$, $p < 0.001$), together with the wider range of plasma volumes in these hypertensive patients than in concurrently studied normal adults (24 to 59 vs. 30 to 50 ml/kg), suggest that the reduced stroke volume and ventricular chamber size in our patients with concentric left ventricular remodeling may reflect cardiac volume underload. A plausible mechanism for this finding is a pressure natriuresis-induced contraction of the intravascular fluid volume, which might account for the relatively mild blood pressure elevation despite severely increased peripheral resistance. Thus, concentric remodeling might reflect the interplay of increased peripheral arterial tone with pressure natriuresis and secondary vascular and ventricular underfilling. Irrespective of its cause, the more cylindric ventricular configuration in patients with concentric remodeling provides a ventricular shape adapted to maximize ventricular contraction during systolic ejection against a high afterload (34).

**Concentric hypertrophy group.** Only a small proportion of hypertensive patients (8% with relative wall thickness above the 99th percentile of normal, or 15% above the 95th percentile partition value) exhibited the typical pattern of concentric hypertrophy, with normal ventricular chamber size and shape and increased muscle mass and relative wall thickness. This group exhibited elevated total peripheral resistance and the highest levels of blood pressure encountered in this study. End-systolic stress was slightly reduced and fractional shortening tended to be high normal, reflecting hypertrophy that was more than adequate to offset rest hemodynamic load.

**Eccentric hypertrophy group.** The fourth group was characterized by eccentric hypertrophy. Although eccentric left ventricular hypertrophy has been observed in hypertension (5,7,25,30,31), it is usually considered to be due to systolic functional impairment (35) or obesity (36–38). In this study, no patient had signs or symptoms of heart failure, which were criteria for exclusion; moreover, fractional shortening was normal despite high end-systolic wall stress, suggesting that important contractile dysfunction was not present in this group, as confirmed by normality of afterload-corrected fractional shortening. Because Doppler ultrasound was not routinely utilized in this study, some regurgitant valvular lesions could have been missed, promoting the development of eccentric hypertrophy in individual patients. However, no clinical evidence of valvular disease was found in our patients, making it highly unlikely that mitral or aortic regurgitation was responsible for this finding. Similarly, obesity did not account for eccentric hypertrophy in the present series because body mass index did not differ among the four groups. As an alternative interpretation, the hemodynamic profile suggests that increased ventricular filling might be responsible for the ventricular dilation, high cardiac output and normal systolic function observed in these patients, possibly through an increase in venous tone (39) or blood volume (33,40), or both. At equivalent blood pressure levels, this group exhibited opposite findings to those associated with concentric remodeling. In the group with eccentric hypertrophy, cardiac index, chamber diameter and end-systolic wall stress were all increased and the left ventricular chamber tended to be more spheric, whereas total peripheral resistance and fractional shortening were normal. Consistent with ventricular chamber size and cardiac index and discordant with blood pressure values, left ventricular mass was normal in the concentric remodeling group and increased in the eccentric hypertrophy group.

**Relation of ventricular geometry to volume load.** These observations are compatible with an important role of cardiac volume load, which affects ventricular chamber size and stroke volume (8,33,41), in contributing to overall load and determining the pattern and extent of myocardial hypertrophy in hypertension. In fact, differences in stroke volume paralleled variations in left ventricular size and geometry. There was a positive linear relation between stroke volume and minor/major hemiaxis ratio (Fig. 3); the concentric remodeling group showed the lowest level of stroke volume and the most elliptic ventricular cavity shape; the group with eccentric hypertrophy exhibited the highest value of stroke volume and the most spheric left ventricle, consistent with the concept that a spheric chamber is best adapted to efficient diastolic filling and a cylindric chamber is best adapted to contraction against a high afterload (34). Patients with normal ventricular geometry or concentric hypertrophy were between these two extremes.

**Clinical implications.** Our findings in a large series of patients with essential hypertension who had not been previously treated indicate that the left ventricle exhibits the geometric patterns of concentric remodeling or eccentric hypertrophy more commonly than it exhibits the pattern of concentric hypertrophy that is considered the typical response to hypertension. However, the latter was found in only 13 (8%) of 165 of our patients when a strict criterion for recognition of elevated relative wall thickness was applied. Recognition of concentric remodeling increased the proportion whose left ventricular geometric abnormalities were detected to 48% from the 35% who had left ventricular hypertrophy based on left ventricular mass index criteria. Examination of measures of systemic hemodynamics and left ventricular load suggest that the lack of increased ventricular mass in patients with concentric remodeling reflected offsetting of the effects of pressure overload by volume underload (reduced stroke volume), whereas concomitant volume and pressure overload contributed to the eccentric hypertrophy observed in about 25% of untreated hypertensive patients. Conversely, concentric hypertrophy seems to be the result of pressure overload and inability to volume underload. These observations suggest that factors able to influence ventricular chamber size or stroke volume (such as blood volume, venous return, afterload, diastolic and inotropic properties) are involved in modulation of left ventricular geometry.

Recent observations from our laboratory (42,43) and from the Framingham Heart Study (44,45) demonstrate that elevated left ventricular mass is a stronger predictor of morbid events or death than is blood pressure or other standard risk factors except age (43–45). Classification of a nonoverlapping group of 253 patients with initially uncomplicated essential hypertension based on the geometric pattern on their initial echocardiogram in our laboratory (43) revealed that the highest risk during a 10-year follow-up period occurred in those with concentric hypertrophy (21% had cardiovascular death, 31% had morbid events) and the lowest risk occurred in those with normal left ventricular geometry (there were no cardiovascular deaths, 11% had morbid events); the risk was intermediate for patients with concentric remodeling and eccentric hypertrophy. Further research will be needed to elucidate both the pathogenesis and the implications for treatment of the spectrum of ventricular patterns in hypertensive patients described in this report.

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